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EXAMINER

SISSON, BRADLEY L.

ART UNIT PAPER NUMBER

1634

DATE MAILED: 11/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/613,903

Applicant(s)

JORDAN, HEATHER J.

Examiner

Bradley L. Sisson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 August 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 43, 44, 46-50, 52-57, 59-61, 63 and 64 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 43, 44, 46-50, 52-57, 59-61, 63 and 64 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____

DETAILED ACTION

Specification

1. The specification is objected to as documents have been improperly incorporated by reference. In particular, the specification states

All publications, patent applications and patents cited herein are fully incorporated by reference herein in their entirety.

Such omnibus language fails to specify what specific information applicant seeks to incorporate by reference and similarly fails to teach with detailed particularity just where that specific information is to be found in each of the cited documents. As set forth in *Advanced Display Systems Inc. v. Kent State University* (Fed. Cir. 2000) 54 USPQ2d at 1679:

Incorporation by reference provides a method for integrating material from various documents into a host document--a patent or printed publication in an anticipation determination--by citing such material in a manner that makes it clear that the material is effectively part of the host document as if it were explicitly contained therein. *See General Elec. Co. v. Brenner*, 407 F.2d 1258, 1261-62, 159 USQP 335, 337 (D.C. Cir. 1968); *In re Lund*, 376 F.2d 982, 989, 153 USPQ 625, 631 (CCPA 1967). **To incorporate material by reference, the host document must identify with detailed particularity what specific material it incorporates and clearly indicate where that material is found in the various documents.** *See In re Seversky*, 474 F.2d 671, 674, 177 USPQ 144, 146 (CCPA 1973) (providing that incorporation by reference requires a statement "clearly identifying the subject matter which is incorporated and where it is to be found"); *In re Saunders*, 444 F.2d 599, 602-02, 170 USPQ 213, 216-17 (CPA 1971) (reasoning that a rejection or anticipation is appropriate only if one reference "expressly incorporates a particular part" of another reference); *National Latex Prods. Co. v. Sun Rubber Co.*, 274 F.2d 224, 230, 123 USPQ 279, 283 (6th Cir. 1959) (requiring a specific reference to material in an earlier application in order to have that material considered a part of a later application); *cf. Lund*, 376 F.2d at 989, 13 USPQ at 631 (holding that **a one sentence reference to an abandoned application is not sufficient to incorporate from the abandoned application into a new application**). (Emphasis added.)

Attention is also directed to MPEP 608.01(p)I, which, in pertinent part, is reproduced below:

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Mere reference to another application, patent, or publication is not an incorporation of anything therein into the application containing such reference for the purpose of the disclosure required by 35 U.S.C. 112, first paragraph. *In re de Seversky*, 474 F.2d 671, 177 USPQ 144 (CCPA 1973). In addition to other requirements for an application, the referencing application should include an identification of the referenced patent, application, or publication. Particular attention should be directed to specific portions of the referenced document where the subject matter being incorporated may be found. (Emphasis added)

2. Accordingly, the cited documents are not considered to have been properly incorporated by reference and as such, have not been considered with any effect towards their fulfilling, either in part or in whole, the enablement, written description, or best mode requirements of 35 USC 112, first paragraph.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 43, 44, 46-50, 52-57, 59-61, 63 and 64 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Attention is directed to the decision in *University of Rochester v. G.D. Searle & Co.* 68 USPQ2D 1424 (Fed. Cir. 2004) at 1428:

To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. *Vas-Cath*, 935 F.3d at 1563; see also *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572 [41 USPQ2d 1961] (Fed. Cir. 1997) (patent specification must describe

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an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention"); *In re Gosteli*, 872 F.2d 1008, 1012 [10 USPQ2d 1614] (Fed. Cir. 1989) ("the description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed"). Thus, an applicant complies with the written-description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572.

5. For convenience, claims 43 and 63, the only independent claims under consideration, are reproduced below.

43. (previously presented) A composition ~~comprising~~ consisting essentially of a plurality of double-stranded DNA fragments of different lengths, wherein fragments of each length are present in an amount that produces bands of substantially equal intensity after the composition is separated by gel electrophoresis and stained with a detectable label.

63. (currently amended) A composition ~~comprising~~ consisting essentially of a plurality of double-stranded DNA fragments of different lengths, wherein fragments of each length are present in an amount that produces bands of substantially equal intensity after the composition is separated by gel electrophoresis and stained with a detectable label, and further ~~comprising~~ consisting essentially of an additional single fragment ~~present in an amount that produces a band visibly brighter than the bands of substantially equal intensity~~ having a relative mass greater than 3 times the relative mass of said bands of substantially equal intensity.

6. For purposes of examination, claims 43 and 63 have been interpreted as encompassing a composition that is virtually limitless in range of sizes of fragments, both in terms of upper and lower limits, and also in terms of differences in sizes of fragments. A review of the disclosure,

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however, fails to find support for such a range of sizes. In support of this position, attention is directed to page 4, last paragraph, bridging to page 5 of the specification, *infra*.

Specifically, the invention relates to nucleic acid ladders or compositions wherein all or substantially all of the bands are substantially equal in intensity and/or wherein all or substantially all of the bands are substantially equal in relative mass. In a preferred aspect of the invention, the compositions or ladders are comprised of nucleic acid fragments in increments of about 1 Kb (kilobase = 1,000 bases or base pairs) (e.g., 1 Kb, 2 Kb, 3 Kb, 4 Kb, 5 Kb etc.) and one or more nucleic acid fragments smaller than 1 Kb (for example, in increments 10 bp, 20 bp, 30 bp, 40 bp, 50 bp, 60 bp, 70 bp, 80 bp, 90 bp 100 bp etc. or any combination thereof); wherein substantially all of the fragments of the ladder or composition are substantially equal in intensity when detected by staining, and/or wherein substantially all of the fragments are substantially equal in relative mass.

Preferably, the nucleic acid ladders and compositions of the invention have two or more bands (preferably four, five, six, seven, eight or more bands) ranging from about 25 Kb to about 100 bp or smaller, preferably 20 Kb to 100 bp, more preferably 15 Kb to 100 bp and most preferably 12 Kb to 100 bp, although smaller ranges are contemplated by the invention.

7. Page 21, second paragraph, states "The product of the invention is illustrated in Figure 2, Lane 1," *infra*.



FIG.2

Figure 2, Lane 1, is construed to contain bands that range in size from about 200 bp to about 10,000 bp, however, the bands from about 500 bp 200 bp in length are considered to be at significantly less intensity than the intensity of bands viewed higher in the gel. Accordingly, the bands from 500 to 200 are not considered to fall within the presently claimed invention, which stipulates that the bands are of "substantially equal intensity." Furthermore, neither the lane, nor any other part of the disclosure has been found to provide an adequate written description of other embodiments of the claimed invention in such full clear and concise language so as to

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reasonably suggest that applicant was in possession of same. As noted above, documents cited above and which have been incorporated by reference improperly, cannot now be relied upon by applicant for fulfillment of either the written description enablement, or best mode requirements of 35 USC 112, first paragraph.

8. It appears that applicant is attempting to satisfy the written description requirement of 35 USC 112, first paragraph, through obviousness. Obviousness, however, cannot be relied upon for satisfaction of the written description requirement. In support of this position, attention is directed to the decision in *University of California v. Eli Lilly and Co.* (Fed. Cir. 1997) 43 USPQ2d at 1405, citing *Lockwood v. American Airlines Inc.* (Fed. Cir. 1997) 41 USPQ2d at 1966:

Recently, we held that a description which renders obvious a claimed invention is not sufficient to satisfy the written description requirement of that invention.

9. In view of the limited disclosure of the specification, and in the absence of convincing evidence to the contrary, claims 43, 44, 46-50, 52-57, 59-61, 63 and 64 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

Response to argument

10. Agreement is reached where at page 9 of the response in that applicant need not provide an example of each and every possible embodiment encompassed by the claims, however, the specification still must provide an adequate written description of the invention not only so one will be able to determine exactly what applicant has, and has not claimed, but to also reasonably suggest that applicant was in possession of the invention. As noted above, it is not enough that alternative embodiments would have been obvious to those of skill in the art. *Ibid.*

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11. At page 9, bridging to page 10 of the response received 30 August 2004 applicant's representative directs attention to pages 4-6 and 8-10 of the specification as providing an adequate written description of the claimed invention.

12. The above argument has been full considered, including review of the cited pages of the disclosure, and has not been found persuasive towards the withdrawal of the rejection. While the various pages do each with detail as to possible increments between bands, as well as the number of copies of a base pair sequence that may be present in a given band, the specification has not been found to provide an adequate written description of an infinite range in base pairs that the bands are comprised of.

13. For the above reasons, and in the absence of convincing evidence to the contrary, claims 43, 44, 46-50, 52-57, 59-61, 63 and 64 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

15. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

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2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

16. Claims 43, 44, 46-50, 52-56, 59-60, 63 and 64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Life Technologies Catalogue (1995-1996).

17. Life Technologies Catalogue discloses for sale a variety of DNA ladders. As seen at page 14-2, the ladder can be comprised of repeating units of 10 bp, and starting from an oligonucleotide of only 10 bp and can go to and beyond 100 bp. Also seen for sale are DNA ladders that are based on repeating units of 50 bp, 100 bp, 123 bp, 1 kb, etc.

18. Life Technologies Catalogue discloses that the concentration of some fragments in some ladders has been adjusted so that certain desired marker(s) appear brighter than others (a limitation of claims 63 and 64). It is also readily apparent that the individual bands in the 1 kb ladder also appear to be at the same relative intensity in the photo of stained bands in a gel subsequent to electrophoresis (see page 14-4). As seen in the caption for the 1 kb ladder, the DNA fragments can be visualized when stained with ethidium bromide (a limitation of claim 55).

19. It would have been obvious to one of ordinary skill in the art at the time the invention was made to have developed any of a variety of DNA ladders for use in an electrophoresis assay and to have adjusted the relative concentrations of the bands such that the intensities of any one or all bands was the same or more intense than others as the ordinary artisan desired. In view of the well-developed state of the art, and the broad usage of such markers, the ordinary artisan would have been both highly motivated and would have had a most reasonable expectation of success.

20. Claims 57 and 61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Life Technologies Catalogue 1995-1996 as applied to claims 43, 44, 46-50, 52-56, 59-60, 63 and 64 above, and further in view of Lee (US patent 5,268,568).
21. See above for the basis of the rejection as it pertains to the disclosure of Life technologies Catalogue 1995-1996.
22. Life Technologies Catalogue 1995-1996 does not disclose the use of the dye mixture.
23. Lee discloses that just a dye mixture comprising bromophenol blue or xylene cyanol FF is routinely added to DNA samples to be subjected to electrophoresis.
24. It would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the DNA ladders of Life Technologies such that a dye comprising bromophenol blue was included given its common usage in electrophoresis of DNA samples. As evidenced by the pictures of the ladders offered for sale by Life technologies, the pictures are of ladders separated via electrophoresis. Accordingly, the addition of a dye to a ladder known to be used in electrophoresis would have been an obvious combination as it would have facilitated the ordinary artisan in determining the degree samples have been subjected to electrophoresis. In view of the commercial availability of DNA ladders, a kit comprising same would have been an obvious commercial expedient, requiring little, if any, additional effort on the part of the ordinary artisan.

Response to argument

25. At page 11 of the response applicant asserts:

The Life Technologies Catalogue does not disclose compositions that consist essentially of bands of substantially the same intensity when separated by gel electrophoresis and stained. A careful examination of the DNA ladders on pages 14-2 through 14-4 of the Life Technologies Catalogue reveals bands of varying intensities within each ladder.

26. The above argument has been fully considered and has not been found persuasive towards the withdrawal of the rejection. As an initial matter, it is noted with particularity that the claims do not proscribe bands being present that are not of the same intensity. Such breadth of scope is achieved by the recitation of “consisting essentially of.” Further, the claims employ the use of the term “substantially” so to impart broader scope into the expression “equal intensity.” Accordingly, the claims fairly encompass compositions where there is to be expected to variance in intensity of the bands, yet they are “of substantial equal intensity” (claim 43).

27. To the extent that there may be one band that is of higher intensity than the others, such is considered to meet the limitation of claim 64, which refers to the presence of an additional “single fragment having a relative mass greater than 3 times the relative mass of said bands of substantially equal intensity.”

28. To the extent that Figure 2, lane 1 exemplifies the claimed invention, it is noted that there is significant variance in the intensity of the bands present.

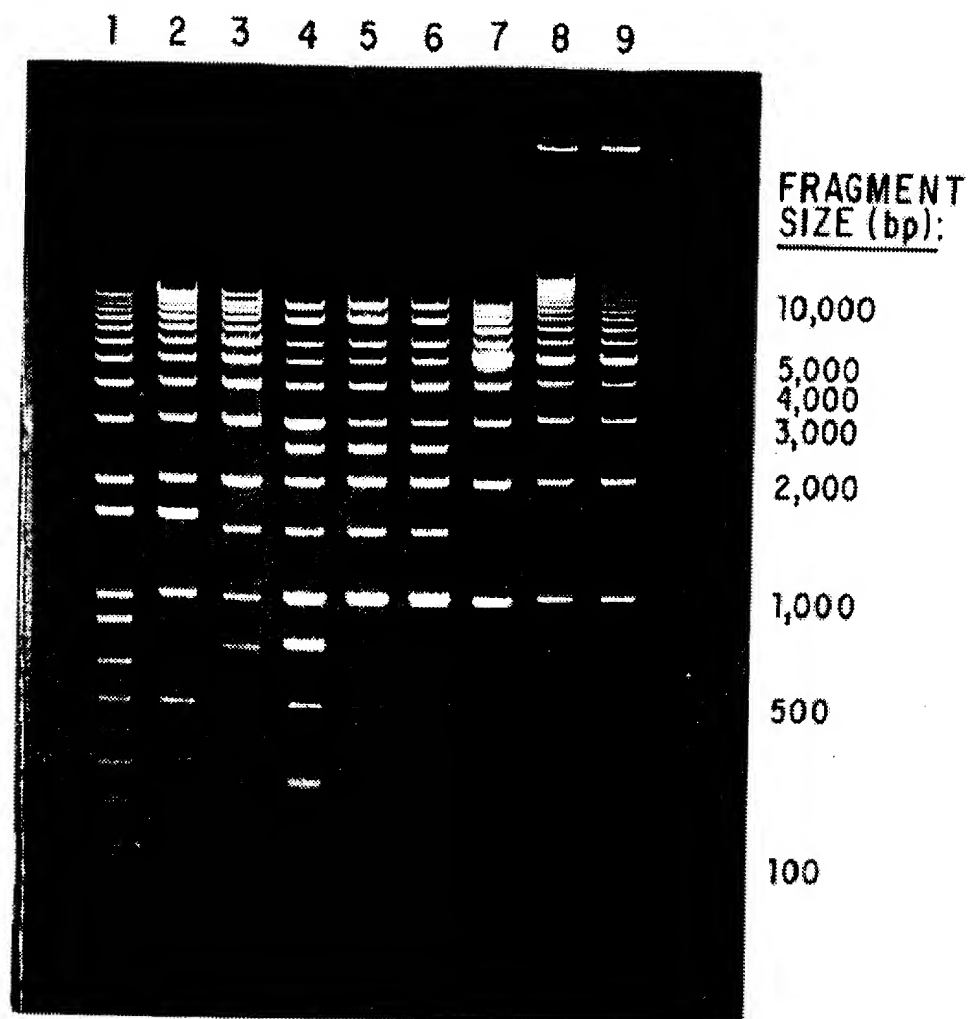


FIG.2

The degree of variance between the bands as found in Lane 1 of Figure 2 is considered to be no less than the degree of variance between bands found in the prior art.

29. It is further noted that there need be only two bands that are of “substantially equal intensity after the composition is separated by gel electrophoresis” (emphasis added).

Accordingly, there need be present only two bands that are of “substantially equal intensity.”

30. Agreement is reached in that the specification does not provide a definition for the expression “substantially equal intensity.” Accordingly, the examiner can adopt a definition of

the term. With the phrase “substantially equal intensity” not being defined, said phrase has been interpreted as allowing for significant variability between bands. Basis for this interpretation is found in the fifth definition of “substantially” as provided by *Merriam-Webster Dictionary*:

5 : being largely but not wholly that which is specified <a *substantial*
lie>

31. Applicant’s representative, at page 12, bridging to page 13 of the response asserts “it is clear that the term “substantially equal intensity” means that the fragment has no more than 3 times the intensity of another fragment.”

32. The above argument has been fully considered and has not been found persuasive as the term has not been defined by the specification as filed. Accordingly, the rejections are maintained.

33. For the above reasons, and in the absence of convincing evidence to the contrary, claims 43, 44, 46-50, 52-56, 59-60, 63 and 64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Life Technologies Catalogue (1995-1996); and claims 57 and 61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Life Technologies Catalogue 1995-1996 as applied to claims 43, 44, 46-50, 52-56, 59-60, 63 and 64 above, and further in view of Lee (US patent 5,268,568).

Conclusion

34. Rejections and/or objections that appeared in the prior Office action and not repeated hereinabove have been withdrawn.

35. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

36. A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

37. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571) 272-0751. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

38. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (571) 272-0745. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

39. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

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system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Bradley L. Sisson
Primary Examiner
Art Unit 1634

BLS
23 November 2004